UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,094	02/26/2004	Susumu Ikehara	Q79949	4252

23373 7590 09/11/2006

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,094	IKEHARA ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-14 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) 1-14 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5/20/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-14 are pending and examined on the merits

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 6-10, 12-14 recite " a third party identical in HLA type". The art recognizes that there are different degrees of identity to HLA haplotype, such as identity at each allele of the HLA-A, B and DR antigen loci which constitute a 6 of 6 "match" (Sykes et al, U.S.6,558,662, column 7, lines 20-26). The allogeneic state is recognized in the art as the condition of having at least one mismatch at a single HLA antigen locus (Dictionary of Immunology, 1985 Herbert et al, Ed.s, page 8 "alloantigen"). It is unclear if applicant intends the identity of HLA to be identical is all six alleles of HLA-A, B and DR, or some degree of mis-match is tolerated in the term "HLA-identical". For purpose of examination, the term HLA-identical will be read as including allogeneic matches.

Claim Rejections - 35 USC § 102

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-7, 10, 12-14 are rejected under 35 U.S.C. 102(e.) as being anticipated by Sykes et al (U.S. 6,558,662).

Claim 1 is drawn to a method for the treatment of malignant tumor which comprises performing donor leukocyte infusion in a patient requiring such treatment and then performing radiation treatment (irradiation), infusion of lymphocytes derived from the host or a third party identical in HLA type to the host, and intra bone marrow-bone marrow transplantation using bone marrow cells derived from the host or a third party identical in HLA type to the host.

Claim 2 embodies the method for the treatment of malignant tumor as defined in claim 1, wherein the donor lymphocyte infusion is for graft versus tumor reaction-based tumor treatment, and the radiation treatment, infusion of lymphocytes derived from the host or a third party identical in HLA type to the host and intra bone marrow-bone marrow transplantation using bone marrow cells derived from the host or a third party identical in HLA type to the host are for the prevention and treatment of the graft versus host disease induced by said donor lymphocyte infusion.

Claim 3 embodies the method for the treatment of malignant tumor as defined in claim 1, wherein a further radiation treatment is performed prior to donor lymphocyte infusion.

Claim 4 embodies the method for the treatment of malignant tumor as defined in claim 1, wherein the donor lymphocyte infusion is performed in the manner of intravenous administration of an effective amount of donor-derived peripheral blood mononuclear cells.

Claim 5 embodies the method for the treatment of malignant tumor as defined in claim 1, wherein the radiation treatment following the donor lymphocyte infusion is performed in the manner of total body irradiation at a dose of 3-4 Gy.

Claim 6 embodies the method for the treatment of malignant tumor as defined in claim 1, wherein the infusion of lymphocytes derived from the host or a third party identical in HLA type to the host is performed in the manner of intravenous administration of an effective amount of peripheral blood mononuclear cells derived form the host or a third party identical in HLA type to the host.

Claim 7 embodies the method for the treatment of malignant tumor as defined in claim 1, wherein the bone marrow cells are whole bone marrow cells derived from the host or a third party identical in HLA type to the host.

Claim 10 is drawn to a method for the treatment of malignant tumor which comprises performing donor lymphocyte infusion for graft versus tumor reaction-based tumor treatment in a patient to be treated and then performing radiation treatment and intravenous administration of peripheral blood stem cells derived from the host or a third party identical in HLA type to the host for the prevention and treatment of the graft versus host disease caused by said donor lymphocyte infusion.

Claim 11 embodies the method for the treatment of malignant tumor as defined in claim 1, wherein the malignant tumor is selected from among leukemia, malignant lymphoma, multiple myeloma, sarcoma, melanoma, brain tumor, stomach cancer, tongue cancer, esophageal carcinoma, colorectal cancer, liver cancer, gallbladder carcinoma, pancreatic carcinoma, renal carcinoma, bladder cancer, nasopharyngeal cancer, laryngeal cancer, skin cancer, mammary cancer, testicular cancer, ovarian cancer, uterus carcinoma, and lung cancer.

Claim 13 is drawn to a method for the prevention and treatment of the graft versus host disease induced by donor lymphocyte infusion which comprises performing, in a patient to be treated for the prevention and treatment of the graft versus host disease, radiation treatment, infusion of lymphocytes derived from the host or a third party identical in HLA type to the host and intra bone marrow-bone marrow transplantation using bone marrow cells derived from the host or a third party identical in HLA type to the host.

Sykes et al disclose a method of treatment of a malignant tumor comprising thymic irradiation, bone marrow transplantation , donor lymphocyte transfusions at days 35 and 56 and thymic irradiation (claim 20, lines 57-67). Sykes et al disclose that the malignant tumor is hematopoietic and comprises leukemias and lymphomas (abstract) which fulfills the specific embodiment of claim 11. Sykes et al disclose that the donor hematopoietic stem cell in the bone marrow transfusion provide hematological function, to induce tolerance to donor antigens, so as to reduce the subject response to any subsequent donor tissue such as donor leukocyte infusion (column 12, lines 41-46 and column 13, lines 52-53). Sykes et al disclose that a state of mixed chimerism is induced by thymic radiation in the subject versus whole body radiation (column 12,

lines 47-50). Sykes et al disclose that the donor leukocytes provides additional graft vs leukemia activity Sykes et al disclose the need for "appropriate" donor leukocyte administration is evidenced by lack of increase in donor chimerism, lack of GVH symptoms or incomplete tumor regression. (column 12, lines 51-59). Sykes et al disclose a delay before the administration of donor leukocyte infusions which allows the host to be less susceptible to GVHD. The donor infusion then converts the mixed chimeric states of the subject into one which is fully chimeric, but the graft cell mediated immune attack will be limited to the hematopoietic compartment thereby minimizing GVHD and maximizing GVL effects (column 12, line 59 to column 13, line 7). Sykes et al disclose the preferred amount of irradiation is preferably less than 400 or 300 rads (column 14, lines 37-48) which corresponds to 3-4 Gy. Sykes et al disclose that bone marrow mismatch at any loci which promotes graft rejection is desirable because said mismatch promotes GVL effects (column 17, lines 24-29). Sykes et al disclose that the disclosed methods can be used when there is a mismatch at a minor histocompatible loci, but it is preferable to be mismatched at a major histocompatibility loci, as in a allogeneic donor (column 17, lines 45-50).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sykes et al (U.S. 6,558,662) in view of Ashkenasy (Stem Cells, 2002, Vol. 20, pp. 86-93).

Claim 8 embodies the method for the treatment of malignant tumor as defined in claim 1, wherein the bone marrow cells are whole bone marrow cells obtained by inserting a bone marrow puncture needle into one end of a long bone of the host or a third party identical in HLA type to the host, causing an irrigating fluid to flow via the needle through the medullary cavity and recovering the irrigating fluid containing bone marrow cells from a perforation provided at the other end of the long bone.

Claim 9 embodies the method for the treatment of malignant tumor as defined in claim 1, wherein the intra bone marrow-bone marrow transplantation is performed in the manner of administration, into a long bone, of an effective amount of whole bone marrow cells derived from the host or a third party identical in HLA type to the host.

Askenasy teaches that isolated limb perfusion and intra-bone marrow transplantation improves the efficiency of the bone marrow graft in non-myeloablated patients (page 87, first column, first full paragraph).

It would have been prima facie obvious at the time the claimed invention was made to do the bone marrow transplantation into the bone of the patient having undergone low-level thymic irradiation. One of skill in the art would have been motivated to do so by the teachings of Askenasy on the improvement in efficiency assoicated with this method of transplanting bone marrow cells into non-myeloablated patients.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
9/5/2006